The past, present and future of stem cell clinical trials for ALS.

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Public Summary:
Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder that is characterized by progressive degeneration of motor neurons in the cortex, brainstem and spinal cord. This degeneration leads to paralysis, respiratory insufficiency and death within an average of 3 to 5 years from disease onset. The mechanisms underlying disease pathology remain unclear and there are no effective treatment options. In recent years, stem cell transplantation therapy has emerged as a potential option for ALS patients. Some ALS treatment studies focus on using stem cells for motor neuron replacement, however this is complicated as the newly replaced motor neurons would not be connected to the muscle in order to affect movement. Alternatively, there is great rationale for using stem cells as support cells to rescue the dying motor neurons that are already connected to the muscle. The motor neuron protection provided by the stem cells could be through reducing inflammation, releasing growth factors, and other potential mechanisms that are not well understood. Prior to moving into patients, stringent pre-clinical studies are required that have a rationale and efficacy in animal models and good safety profiles. However, given our poor understanding of what causes ALS and whether stem cells may ameliorate symptoms, there should be a push to determine cell safety in pre-clinical models and then a quick move to the clinic where patient trials will show if there is any efficacy. Here, we provide a critical review of current clinical trials using either mesenchymal or neural stem cells to treat ALS patients. Pre-clinical data leading to these trials, as well as those in development are also evaluated in terms of mechanisms of action, validity of conclusions and rationale for advancing stem cell treatment strategies for this devastating disorder.

Scientific Abstract:
Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder that is characterized by progressive degeneration of motor neurons in the cortex, brainstem and spinal cord. This leads to paralysis, respiratory insufficiency and death within an average of 3 to 5years from disease onset. While the genetics of ALS are becoming more understood in familial cases, the mechanisms underlying disease pathology remain unclear and there are no effective treatment options. Without understanding what causes ALS it is difficult to design treatments. However, in recent years stem cell transplantation therapy has emerged as a potential new way to deliver relief to ALS patients. While motor neuron replacement remains a focus of some studies trying to treat ALS with stem cells, there is more rationale for using stem cells as support cells for dying motor neurons as they are already connected to the muscle. This could be through reducing inflammation, releasing growth factors, and other potential mechanisms that are not well understood. Prior to moving into patients, stringent pre-clinical studies are required that have at least some rationale and efficacy in animal models and good safety profiles. However, given our poor understanding of what causes ALS and whether stem cells may ameliorate symptoms, there should be a push to determine cell safety in preclinical models and then a quick move to the clinic where patient trials will show if there is any efficacy. Here, we provide a critical review of current clinical trials using either mesenchymal or neural stem cells to treat ALS patients. Pre-clinical data leading to these trials, as well as those in development are also evaluated in terms of mechanisms of action, validity of conclusions and rationale for advancing stem cell treatment strategies for this devastating disorder.